

Remarks

Claims 42-48, 52-56, 59, 62-66, 69, 72-77, 80, 83, 86-89 and 92-94 are presently pending in the instant application. Claims 43-45 are objected to as being dependent on a rejected base claim. Claims 42, 46-48, 52-56, 59, 62-66, 69, 72-77, 80, 83, 86-89 and 92-94 are rejected.

In the specification, the paragraph spanning lines 21-36 on page 39 has been rewritten so as to correctly identify the number of amino acid residues deleted from the N-terminus of the TNF- γ - α polypeptide in the creation of the construct pQE60TNFg-3/147. Support for this amendment lies in the knowledge that one of skill in the art would be able to properly calculate the correct numbers of amino acids deleted given the description of constructs given in this paragraph and the amino acid sequence of SEQ ID NO:2.

Claims 51, 84 and 85 have been canceled without prejudice or disclaimer.

Claims 42-48, 52, 55, 56, 59, 62, 65, 66, 69, 72, 75, 77, 80, 83, 86, 89 and 92 have been amended to more specifically point out and distinctly claim certain embodiments of the present invention. Support for amendments to claim 42 is found, for example, at page 6, lines 10-19; page 36, lines 18-24; and at page 50, lines 35-37. Support for amendments to the remaining claims are found throughout the specification as originally filed.

Therefore, no new matter has been added. Accordingly, Applicants respectfully request that the amendments and remarks of the present response be entered and made of record in the present application

I Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

A. The Examiner has rejected claims 42, 46-48, 51-55, 59, 62-65, 69 and 72-74, under 35 U.S.C. § 112, first paragraph, as allegedly containing "subject matter which was

not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.”
See, Paper No. 25, page 2.

Preliminarily, Applicants note that presently rejected claim 51 has been canceled without prejudice or disclaimer. Accordingly, the present rejection will be addressed in so far as it is understood by Applicants to apply to remaining pending claims.

Applicants have transmitted herewith a Statement by Attorney for Applicants Regarding Permanence and Availability of Deposited Plasmids, which states that the claimed cDNA was accepted by an International Depositary Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon grant of a patent on this application.

In light of the statement made by Applicants’ Attorney and the above remarks, Applicants respectfully request that the rejection of pending claims 42, 46-48, 52-55, 59, 62-65, 69 and 72-74, under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

B. The Examiner has rejected claim 56, under 35 U.S.C. § 112, first paragraph, as allegedly containing “subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” *See*, Paper No. 25, page 4.

Applicants have herein amended claims 56 and 59 to recite “encoded by a polynucleotide which consists of”, thereby obviating the present rejection. Accordingly, Applicants respectfully request that the rejection of claim 56, under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Written Description

The Examiner has rejected claims 42, 51-56, 59, 62-66, 69, 72-76, 86-89 and 92-94, under 35 U.S.C. § 112, first paragraph, as allegedly containing "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the invention." *See*, Paper No. 25, page 4.

The Examiner further alleges that "the claims do not require that the polypeptide possess a particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity or partial sequence identity." *See*, Paper No. 25, page 5. The rejection is respectfully traversed. Applicants assert that each of the claims pending prior to and after the present amendment is fully supported and satisfies the statutory written description requirements under 35 U.S.C. § 112.

Preliminarily, Applicants note that presently rejected claim 51 has been canceled without prejudice or disclaimer. Accordingly, the present rejection will be addressed in so far as it is understood by Applicants to apply to remaining pending claims.

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, Applicants maintain that the Examiner has not met this burden.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention based on the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Indeed, as the Federal Circuit has noted, “the issue is whether one of skill in the art could derive the claimed ranges from the patent’s disclosure.” *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000) (emphasis added).

Claims 42, 51-56, 59, 62-66, 69, 72-76, 86-89 and 92-94 stand rejected because polypeptides encompassed by the present claims are alleged not to be functionally or structurally limited beyond the amino acid sequence. Further, the Examiner alleges that the claims “do not place any limit on the number or type of amino acid substitutions, deletions, insertions and/or additions that may be made to the claimed polypeptide.” See, Paper No. 25, page 5.

It is well established that a “gene is a chemical compound, albeit a complex one”. *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to particular polypeptides of the disclosed amino acid sequence of SEQ ID NO:2, as encoded by the nucleic acid sequence of SEQ ID NO:1, are essentially chemical claims involving generic chemical formulae. As stated by Judge Lourie in *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), “In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.” All of the objectives met by a generic chemical formula are similarly met by the explicit

description in the instant specification of a polynucleotide sequence (*i.e.* SEQ ID NO:1) and the amino acid sequence encoded thereby (SEQ ID NO:2) and by the instant claims to polypeptides consisting of the full-length, full-length minus N-terminal methionine, and mature polypeptides having the amino acid sequence of SEQ ID NO:2; the full-length, full-length minus N-terminal methionine, and mature polypeptides having the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 75927; polypeptides consisting of at least 10 or 30 amino acids of SEQ ID NO:2; polypeptides having a recited percent identity to SEQ ID NO:2; and polypeptides encoded by polynucleotides which hybridize to SEQ ID NO:1. That is, the instant claims clearly distinguish the boundaries of the claimed genera and identify all of the members of those genera. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims upon reading the present application as filed, and would immediately recognize that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563). Therefore, the specification contains an adequate written description of the claimed polypeptides. Applicants have provided the skilled artisan with a "generic formula" in the form of the amino acid sequence of SEQ ID NO:2, which indicates "with specificity what the generic claims encompass." Armed with this information "one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass."

Furthermore, the specification particularly discloses embodiments of the invention rejected by the Examiner in the present action. Polypeptides consisting of at least 30 amino acid residues of SEQ ID NO:2 are disclosed, for example, at page 7, lines 6-12; polypeptides having at least 90% identity to SEQ ID NO:2 are disclosed, for example, at Page 41, lines 7-14; and polynucleotides which hybridize to polynucleotides of SEQ ID

NO:1 or polynucleotides encoding the amino acid sequence of SEQ ID NO:2 are disclosed, for example, at Page 25, line 23 through Page 26, line 17. Accordingly, one skilled in the art, enlightened by the teachings of the present application, could readily envision all of the various polynucleotide sequences that comprise the specified polynucleotides.

For example, the skilled artisan could clearly envision each of the polypeptides comprising at least 30 contiguous amino acids, of SEQ ID NO:2 as a progression, *i.e.*, polypeptides comprising amino acids 1-30, 2-31, 3-32, etc. The skilled artisan could certainly further envision sequentially adding contiguous amino acids to either end of any of the described embodiments. Indeed, nothing more than what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides and polypeptide fragments containing at least 30 amino acids of SEQ ID NO:2. Likewise, the skilled artisan could easily substitute any given nucleotide for any other given nucleotide, or add or delete nucleotides, such that nothing more than what is described in the specification would be required to identify every single one of the polypeptides comprising amino acid sequences that are at least 90% identical to the amino acid sequence of SEQ ID NO:2. Thus, it would be readily apparent to the skilled artisan that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563).

For all of the above reasons, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully

request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

The Examiner has failed to provide any showing that one skilled in the art would *not* reasonably conclude that Applicants possessed the claimed subject matter as of the priority date of the present application. Applicants respectfully submit that the entire claimed genus of polypeptides is described such that a skilled artisan would recognize that Applicants were in possession of the genus. Further, because the claims recite polypeptides which consist of portions of the amino acid sequence of SEQ ID NO:2, the claims do not read on undescribed amino acid sequences. Accordingly, the Examiner's rejection under 35 U.S.C. § 112, first paragraph, for lack of adequate description should be withdrawn.

Accordingly, Applicants respectfully request that the rejection of claims 42, 52-56, 59, 62-66, 69, 72-76, 86-89 and 92-94, under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, be reconsidered and withdrawn.

II Rejections Under 35 U.S.C. § 112, second paragraph

A. The Examiner has rejected claims 42, 48, and 51-54, under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite because they recite the term "mature"." *See*, Paper No. 25, page 7.

Applicants respectfully point out that claim 51 has been cancelled without prejudice or disclaimer, thereby obviating its rejection. Furthermore, in the interest of advancing prosecution and not in acquiescence to the Examiner's assertion, claims 42 and 48, as well as all claims dependent therefrom, have been amended to no longer recite the term "mature." Accordingly, Applicants respectfully request that the present rejection of

claims 42, 48, and 52-54 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

B. The Examiner has rejected claims 42, 51-56, 59, 62-66, 69, 72-77, 80, 83-89 and 92-94, under 35 U.S.C. § 112, second paragraph, as allegedly being “indefinite because they recite either the term “specifically binds” or “specific for”.” *See*, Paper No. 25, page 7.

Applicants respectfully point out that claims 51, 84 and 85 have been cancelled without prejudice or disclaimer, thereby obviating its rejection. Furthermore, in the interest of advancing prosecution and not in acquiescence to the Examiner’s assertion, claims 42, 52-56, 59, 62-66, 69, 72-77, 80, 83, 86-89 and 92-94 have been amended to no longer recite “specifically binds” or “specific for.” Accordingly, Applicants respectfully request that the present rejection of claims 42, 52-56, 59, 62-66, 69, 72-77, 80, 83, 86-89 and 92-94 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

C. The Examiner has rejected claims 51, 84 and 85, under 35 U.S.C. § 112, second paragraph, as allegedly being “indefinite because they recite the term “TNF- γ - α ”.” *See*, Paper No. 25, page 7.

Applicants respectfully point out that claims 51, 84 and 85 have been cancelled without prejudice or disclaimer, thereby obviating its rejection. Accordingly, Applicants respectfully request that the present rejection of claims 51, 84 and 85 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

D. The Examiner has rejected claim 84, under 35 U.S.C. § 112, second paragraph, as allegedly being “indefinite because it recites the term “TNF- γ - α activity”.” *See*, Paper No. 25, page 7.

Applicants respectfully point out that claim 84 has been cancelled without prejudice or disclaimer, thereby obviating its rejection. Accordingly, Applicants respectfully request that the present rejection of claims 84 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

III Claim Objections

The Examiner has objected to claims 51 and 85, as allegedly being of improper dependent form. (*See*, Paper No. 25, page 8). Specifically, the Examiner alleges that “[a] fragment of polypeptide that binds an antibody specific for TNF- γ - α fails to further limit a fragment of polypeptide, respectively, that specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.” *Id.*

Applicants respectfully point out that claims 51 and 85 have been cancelled without prejudice or disclaimer, thereby obviating this objection. Accordingly, Applicants respectfully request that the present objection to claims 51 and 85 be reconsidered and withdrawn.

IV Specification

The Examiner has objected to the amendment filed on September 26, 2001, under 35 U.S.C. § 132, as allegedly introducing new matter into the specification. (*See*, Paper No. 25, page 8). Specifically, the Examiner objects to the alleged introduction of “U034070” into the paragraph bridging lines 20-27 at page 10, and the alleged introduction of “24” into the paragraph bridging lines 21-36 at page 39. *Id.* Applicants respectfully disagree and traverse this objection.

Applicants note that “U034070,” in the amended paragraph bridging lines 20-27 at page 10, merely corrects the GenBank identifier of a sequence already contained in Figure 2, and in the sequence listing of the application as originally filed. Therefore, Applicants

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contend that "U034070" simply serves to provide the public with the source reference for publicly available information used in the preparation of the present application. Furthermore, armed with the specification of the application as originally filed, one of ordinary skill in the art would have been able to routinely use sequence information to search publicly available databases and determine that "U034070" was the correct GenBank identifier for the sequence at issue. Accordingly, Applicants respectfully contend that "U034070" does not constitute new matter, and request that the Examiner's objection be reconsidered and withdrawn.

Applicants note that the paragraph bridging lines 21-36 at page 39 has been further amended to no longer recite "24" thereby obviating the Examiner's objection. Accordingly, Applicants respectfully request that the Examiner's objection be reconsidered and withdrawn.

V Rejections Under 35 U.S.C. § 102

The Examiner has rejected claims 42, 51, 52 and 54, under 35 U.S.C. § 102(b), as allegedly being anticipated by Park (EP-0403114-A1, December 1990) in view of Benjamini (Immunology: A Short Course. Wiley-Liss, Inc., New York. July 1991). Specifically, the Examiner alleges that the Park reference discloses a seven (7) contiguous amino acid residue fragment of SEQ ID NO:2 of the present application, and the Benjamini reference indicates that an epitope is approximately equal to 5-7 amino acid residues. (*See*, Paper No. 25, pages 9-10).

Preliminarily, Applicants note that presently rejected claim 51 has been canceled without prejudice or disclaimer. Furthermore, claim 42 has been amended so as to no longer recite "a fragment of the polypeptide" thereby obviating its rejection as anticipated by the Park reference in view of Benjamini. The present amendment further obviates the

present rejection of claims 52 and 54, each of which claims depends from amended claim 42.

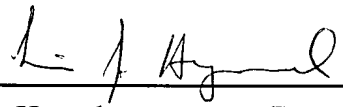
Accordingly, Applicants respectfully request that the present rejection of claims 42, 52 and 54, under 35 U.S.C. § 102(b), be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the amendment and remarks of the present response be entered and made of record in the present application. The present application is believed to be in condition for allowance. Early notice to that effect is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below. If a fee is required in connection with this paper, please charge Deposit Account No. 08-3425 for the appropriate amount.

Respectfully submitted,

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Lin J. Hymel (Reg. No. 45,414)
Attorney for Applicants
Human Genome Sciences, Inc.
9410 Key West Avenue
Rockville, MD 20850
(301) 251-6015 (phone)

Enclosures
KKH/LJH/BM/lcc

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Yu et al.

Attorney Docket No.: PF141P4

Application Serial No.: 09/246,129

Art Unit: 1647

Filed: February 8, 1999

Examiner: Romeo, D.

Title: TUMOR NECROSIS FACTOR-GAMMA

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

The entire paragraph spanning lines 21-36 on page 39 has been replaced by the following rewritten paragraph:

The remaining TNF-gamma-alpha expression constructs were used to express various TNF-gamma muteins from bacterial, baculoviral, and mammalian systems. Four N-terminal deletion mutations have been generated using the pQE60 bacterial expression vector. These N-terminal deletion mutation constructs are: (i) pQE60TNFg-3/147 (representing a possible mature TNF-gamma polypeptide; the polypeptide expressed by this construct is identical to amino acid residues 107-251 of the TNF-gamma-beta of SEQ ID NO:20), (ii) pQE60TNFg12/147 (representing amino acid residues 12-147 of SEQ ID NO:2 and residues 116-251 of SEQ ID NO:20), (iii) pQE60TNFg22/147 (representing amino acid residues 22-147 of SEQ ID NO:2 and residues 126-251 of SEQ ID NO:20), and (iv) pQE60TNFg28/147 (representing amino acid residues 28-147 of SEQ ID NO:2 and residues 132-251 of SEQ ID NO:20). Each of these expression constructs can be used to produce a TNF-gamma polypeptide in a bacterial system which exhibits an N-terminal deletion of ~~24~~ 29, 38, 48 and 54 amino acids, respectively, with regard to the full-length

TNF-gamma-alpha polypeptide or an N-terminal deletion of 106, 115, 125, and 131 amino acids, respectively, with regard to the full-length TNF-gamma-beta polypeptide.

In The Claims

Claims 51, 84 and 85 have been canceled without prejudice or disclaimer.

Claims 42-48, 52, 55, 56, 59, 62, 65, 66, 69, 75, 77, 80, 83, 86, 89 and 92 have been replaced with the following rewritten claims:

--42. (Twice Amended) An isolated polypeptide ~~comprising~~ consisting of an amino acid sequence selected from the group consisting of:

(a) amino acid residue -27 to amino acid residue +147 as set forth in SEQ ID NO:2;

(b) amino acid residue -26 to amino acid residue +147 as set forth in SEQ ID NO:2;

(c) amino acid residue +1 to amino acid residue +147 as set forth in SEQ ID NO:2;

~~(d) a fragment of the polypeptide of SEQ ID NO:2, wherein the fragment specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2;~~

(ed) a full-length polypeptide having the amino acid sequence expressed by the cDNA plasmid contained in ATCC Deposit No. 75927;

(fe) a full-length polypeptide, excluding the N-terminal methionine residue, having the amino acid sequence expressed by the cDNA plasmid contained in ATCC Deposit No. 75927; and

(gf) a ~~mature~~ polypeptide having the amino acid sequence expressed by a recombinant cell comprising the cDNA plasmid contained in ATCC Deposit No. 75927; and

~~(h) a fragment of the polypeptide having the amino acid sequence expressed by the cDNA plasmid contained in ATCC Deposit No. 75927, wherein the fragment specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

43. (Once Amended) The isolated polypeptide of claim 42 ~~comprising~~ consisting of amino acid residue -27 to amino acid residue +147 as set forth in SEQ ID NO:2.

44. (Once Amended) The isolated polypeptide of claim 42 ~~comprising~~ consisting of amino acid residue -26 to amino acid residue +147 as set forth in SEQ ID NO:2.

45. (Once Amended) The isolated polypeptide of claim 42 ~~comprising~~ consisting of amino acid residue +1 to amino acid residue +147 as set forth in SEQ ID NO:2.

46. (Once Amended) The isolated polypeptide of claim 42 ~~comprising~~ consisting of a full-length polypeptide having the amino acid sequence expressed by the human cDNA contained in ATCC Deposit No. 75927.

47. (Once Amended) The isolated polypeptide of claim 42 ~~comprising~~ consisting of a full-length polypeptide, excluding the N-terminal methionine residue, having the amino acid sequence expressed by the human cDNA contained in ATCC Deposit No. 75927.

48. (Once Amended) The isolated polypeptide of claim 42 ~~comprising~~ consisting of a ~~mature~~-polypeptide having the amino acid sequence expressed by a recombinant cell comprising the human cDNA contained in ATCC Deposit No. 75927.

52. (Once Amended) The isolated polypeptide of claim 42 wherein said polypeptide ~~further comprises~~ is fused to a heterologous polypeptide.

55. (Thrice Amended) An isolated polypeptide encoded by a nucleic acid molecule ~~comprising~~ consisting of a polynucleotide sequence selected from the group consisting of:

(a) a polynucleotide sequence of at least 30 contiguous nucleotides of nucleotides 783 to 1304 of SEQ ID NO:1; and

(b) a polynucleotide sequence of at least 30 contiguous nucleotides of the open reading frame encoded by the cDNA plasmid contained in ATCC Deposit No. 75927;

~~wherein said polypeptide specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

56. (Once Amended) The isolated polypeptide of claim 55 encoded by a polynucleotide which ~~comprises~~ consists of (a).

59. (Once Amended) The isolated polypeptide of claim 55 encoded by a polynucleotide which ~~comprises~~ consists of (b).

62. (Once Amended) The isolated polypeptide of claim 55 wherein said polypeptide ~~further comprises~~ is fused to a heterologous polypeptide.

65. (Twice Amended) An isolated polypeptide ~~comprising~~ consisting of an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence ~~comprising~~ consisting of at least 30 contiguous amino acid residues of SEQ ID NO:2; and

(b) an amino acid sequence ~~comprising~~ consisting of at least 30 contiguous amino acid residues encoded by the cDNA plasmid contained in ATCC Deposit No. 75927;

~~wherein said polypeptide specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

66. (Once Amended) The isolated polypeptide of claim 65 which ~~comprises~~ consists of (a).

69. (Once Amended) The isolated polypeptide of claim 65 which ~~comprises~~ consists of (b).

72. (Once Amended) The isolated polypeptide of claim 65 wherein said polypeptide ~~further comprises~~ is fused to a heterologous polypeptide.

75. (Thrice Amended) An isolated polypeptide ~~comprising~~ consisting of a first amino acid sequence 90% or more identical to a second amino acid sequence selected from the group consisting of:

(a) a second amino acid sequence ~~comprising~~ consisting of amino acid residues -27 to 147 of SEQ ID NO:2;

(b) a second amino acid sequence ~~comprising~~ consisting of amino acid residues -26 to 147 of SEQ ID NO:2; and

(c) a second amino acid sequence ~~comprising~~ consisting of amino acid residues 1 to 147 of SEQ ID NO:2;

~~wherein said polypeptide specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

77. (Once Amended) The isolated polypeptide of claim 75 which ~~comprises~~ consists of second amino acid sequence (a).

80. (Once Amended) The isolated polypeptide of claim 75 which ~~comprises~~ consists of second amino acid sequence (b).

83. (Once Amended) The isolated polypeptide of claim 75 which ~~comprises~~ consists of second amino acid sequence (c).

86. (Once Amended) The isolated polypeptide of claim 75 wherein said polypeptide ~~further comprises~~ is fused to a heterologous polypeptide.

89. (Thrice Amended) An isolated polypeptide encoded by a nucleic acid molecule ~~comprising~~ consisting of a polynucleotide which hybridizes to the complement of the polynucleotide set forth in nucleotides 783-1304 of SEQ ID NO:1 wherein said hybridization occurs under conditions comprising hybridization in a buffer consisting of 50% formamide, 5x SSC, 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA at 42°C and wash in a solution consisting of 0.1x SSC at 65°C and said polypeptide has proinflammatory activity, ~~wherein said polypeptide specifically binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

92. (Once Amended) The isolated polypeptide of claim 89 wherein said polypeptide ~~further comprises~~ is fused to a heterologous polypeptide.--